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OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

**MEMORANDUM**

DATE: 25 JANUARY 2011

SUBJECT: FIPRONIL – Exposure/Risk Assessment for the Proposed New Use of Fipronil Applied as a Dry Aerosol Spray for Termite Control.

PC Code: 129121 CASRN: 120068-37-3 DP Code: 385945

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## INTRODUCTION

Under provisions in Section 3 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, the BASF Corporation and the Whitmire Micro-Gen Research Laboratories, Inc. have requested registration of the insecticide active ingredient (ai) fipronil (PC No. 129121; CAS No. 120068-37-3) for use as a termiticide applied as a dry aerosol spray product from pressurized cans.

The risk assessment techniques used in this document are those that have been developed and refined by the HED/Office of Pesticide Programs' Science Policy Council for Exposure (ExpoSAC). RD herein utilizes the same techniques as are HED's standard operating procedures (SOP).



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Recd 1-26-11

## USE PATTERN SUMMARY

The product proposed for registration is designated at TC-309. A proposed alternate brand name is "Prescription Treatment® Brand Termidor® Dry Pressurized" (EPA Reg. No. 7969-XXX). It is formulated as a dry, aerosol spray delivered from pressurized spray cans. The spray cans contain a net weight of 8 fl oz of which 0.05 % is active ingredient fipronil It should be noted that fipronil is currently registered for use as a termiticide (Termidor® 80 WG Termiticide/Insecticide, Reg. No. 7969-209; Termidor® SC Termiticide/Insecticide, Reg. No. 7969-210).

According to the draft product label (v1.0 (9/28/10; dmt)), "This product is a ready-to-use insecticide formulation containing fipronil. When dispersed, the formulation rapidly disperses into voids, carton, and insect galleries. It is designed to be placed into insect galleries, cartons, voids, other wooden members of structures, landscaped timbers or trees where listed termites are active or suspected. Dispense 1-3 seconds of product per application depending on the size of the gallery, carton, harborage or void. For trees or larger voids, dispense 1-10 seconds per site. The highest rate is typically used for treating carton or large voids in trees. Wait 3-5 seconds before removing actuator tip after finishing application. This product can be applied in and around elements that are subject to attack by, or provide harborage to termites. Applications can be made from the interior and/or exterior. Drilling of hole(s) may be required to access galleries or harborages. Treatment of insect harborages associated with trees, shrubs, utility poles, fences, bridges, landscape timbers, under slabs or other non-structural elements permitted."

The proposed (draft) label further states: "This treatment is intended for localized infestations only. The purpose of such applications is to kill termites which may be present in the treated channels at the time of treatment or reenter the area at a later date. Such applications are intended as supplemental treatment to, but not a substitute for, mechanical alteration, soil treatment, or foundation treatment."

## OCCUPATIONAL PESTICIDE HANDLER EXPOSURE

Based upon the proposed use pattern, RD believes the most highly exposed occupational pesticide handlers will be applicators using the pressurized spray cans.

No chemical specific exposure data were available with which to estimate possible occupational exposure. The estimates of exposure are based upon information in the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (v. 1.1, August 1998) as cited in the Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments (18 DEC 1997, page B-5). The proposed label does not mention the suggested use of personal protective equipment. The "Unit Exposure" taken from the PHED is for an "applicator" wearing short pants, short-sleeved shirt and no protective gloves. Thus, RD expects the estimate of exposure is likely to be an "upper-bound" estimate.

Since no information is available with regards to a "typical" application, RD assumes an applicator is exposed to the entire contents (8.0 fl oz) of a spray can(s). The product density is 7.413 lb/gal. Therefore, 7.413 lb/gal ÷ 128 fl oz/gal = 0.0579 lb/fl oz. Since there are 8.0 fl

oz/can, 8.0 fl oz/can * 0.0579 lb/fl oz = 0.463 lb/can. And since the product contains 0.05 % active fipronil, then, 0.463 lb/can * 0.0005 active fipronil = 0.000232 lb active fipronil/can.

The toxicological factors used in this assessment are taken from: Memorandum, 10 March 2010, M. Dow, " FIPRONIL – Nondietary Exposure/Risk Assessment for the Proposed Use of Fipronil in Termidor® Dry Termiticide.", DP Code 372250.

The Agency identified a short-term duration (1 - 30 days) dermal toxicological endpoint from a 21-day dermal toxicity study in the rabbit. The No Observable Adverse Effects Level (NOAEL) is 5.0 mg ai/kg bw/day and the toxic effects noted were decreased body weight gain and food consumption in both sexes. A 70 kg body weight is used to calculate exposure and dose from dermal exposure. Since the dermal toxicological endpoint was identified from a dermal study, there is no adjustment for dermal absorption. The level of concern (LOC) for dermal exposures is for Margins of Exposure (MOE) < 100.

A short-term duration inhalation endpoint was identified from a developmental neurotoxicity study in the rat. The NOAEL is 0.05 mg ai/kg bw/day and the toxic effects seen were decreases in group mean pup weights during lactation and significant increase in time of preputial separation in males. Since the inhalation toxic effects were identified from a developmental study with fetal effects, a 60 kg bw is used to calculate inhalation exposure. HED and RD assume 100% absorption via the inhalation route of exposure. See Table 1.0 for a summary of estimated exposures and risks and see the ATTACHMENT for a summary of toxicological endpoints used for risk assessment.

RD has no credible information with regards to how many containers might be used (i.e., applied by an individual) in a given work day. Further, there is no information as to what fraction of a container might typically be used in a given work day. Therefore, for purposes of a Tier I or "screening" level assessment, RD presents estimates of exposure and risk that might result from applying 1, 5 or 10 containers in a given work day.

In cases where dermal and inhalation NOAELs are identified from different studies and cite different toxicological responses, HED uses the following convention to "combine" dermal and inhalation exposures: $\frac{1}{(1/MOE_{dermal}) + (1/MOE_{inhalation})}$.

| Table 2.0 Summary of Exposure & Risk to Occupational Handlers From Fipronil Applied From Pressurized Aerosol Spray Cans | | | | |
|---|---|---|---|---|
| **Unit Exposure[1]** mg ai/lb handled | **Applic. Rate[2]** lb ai/unit | **Units Treated[3]** | **Avg. Daily Exposure[4]** mg ai/kg bw/day | **MOE[5]** |
| ***Applicator - Pressurized Spray Can*** | | | | |
| Dermal: SLNoGlove 220.0<br>Inhal. 2.4 | 0.000232 lb ai/can | 1 can/day | Dermal: SLNoGlove 0.000729<br>Inhal. 0.00000928 | 6859<br>5388<br>Combined 3000 |
| ***Applicator - Pressurized Spray Can*** | | | | |
| Dermal: SLNoGlove 220.0<br>Inhal. 2.4 | 0.000232 lb ai/can | 5can/day | Dermal: SLNoGlove 0.00365<br>Inhal. 0.0000464 | 1369<br>1077<br>Combined 600 |
| ***Applicator - Pressurized Spray Can*** | | | | |
| Dermal: SLNoGlove 220.0<br>Inhal. 2.4 | 0.000232 lb ai/can | 10can/day | Dermal: SLNoGlove 0.00729<br>Inhal. 0.0000928 | 686<br>538<br>Combined 300 |

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing – Short pants, short-sleeved shirt, shoes plus socks No protective gloves; Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled.
2. Applic. Rate. = assumed and derived from label information..
3. Units Treated are assumed.
4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated ÷ kg Body Weight (70 kg for dermal; 60 kg for inhalation.
5. MOE = Margin of Exposure = NOAEL ÷ ADD. Dermal NOAEL = 5.0 mg/kg bw/day; Inhalation NOAEL = 0.05 mg/kg bw/day

In cases where dermal and inhalation NOAELs are identified from different studies and cite different toxicological responses, HED uses the following convention to "combine" dermal and inhalation exposures:

$$\frac{1}{(1/MOE_{dermal}) + (1/MOE_{inhalation})}.$$

A MOE of 100 is adequate to protect occupational pesticide handlers from exposures to fipronil. The estimated MOEs are all > 100 and are based upon conservative assumptions i.e., that short pants and short-sleeved shirt are worn without protective gloves AND that the operator is exposed to the entire content(s) of active ingredient per can(s). The estimates are considered conservative thus protective. Therefore the proposed new uses do not exceed RD's level of concern.

## POST-APPLICATION EXPOSURE TO AGRICULTURAL WORKERS

Typically, for most pesticide application systems, there is the possibility of post-application exposure. In this case, post-application exposure is believed to be negligible. The material is injected **into** the substrate being treated i.e., structures, nests, cartons etc. Little if any, is expected to remain on the treatment surface. Even if material does exist on the surface of the substrate that was treated, RD does not expect the exposure to equal or exceed what has been estimated for occupational handlers i.e., applicators. The estimates of applicator exposure are very conservative and it does not seem possible, practically speaking, for post-application exposure to exceed the Agency's level of concern.

# ATTACHMENT

**Acute Toxicity Data on *FIPRONIL***

| Guideline No./ Study Type | MRID No. | Results | Toxicity Category |
|---|---|---|---|
| 870.1100 Acute oral toxicity -rat | 42918628 | LD50 = _ 92/_ 103 mg/kg; _+_ 97 mg/kg | II |
| 870.1200 Acute dermal toxicity | 42918629<br>42918630 | LD50 = > 2000 mg/kg [rat]<br>= 354 mg/kg [rabbit] | III<br>II |
| 870.1300 Acute inhalation toxicity -rat | 43544401 | LC50 = _ 0.36/_ 0.42 mg/L; _+_ 0.39 mg/L | II |
| 870.2400 Acute eye irritation -rabbit | 42918632 | mild transient ocular irritant | III |
| 870.2500 Acute dermal irritation - rabbit | 42918633 | slight dermal irritant | IV |
| 870.2600 Skin sensitization -Guinea Pig | 42918634 | non-sensitizing | |

**Summary of Toxicological Dose and Endpoints for Fipronil for Use in Human Risk Assessment [1].**

| Exposure Scenario (Fipronil) | Dose Used in Risk Assessment, UF | FQPA SF and Endpoint for Risk Assessment | Study and Toxicological Effects |
|---|---|---|---|
| Acute Dietary<br>all populations<br>including infants and children | NOAEL= 2.5 mg/kg<br>UF = 100<br>**Acute RfD** = 0.025 mg/kg | FQPA SF = 1<br>**aPAD** = acute RfD / FQPA SF<br>= 0.025 mg/kg | Acute neurotoxicity - rat<br>LOAEL = 7.0 mg/kg based on: decreased hindleg splay in males at 7 hours. |
| Chronic Dietary<br>all populations | NOAEL= 0.019 mg/kg/day<br>UF = 100<br>**Chronic RfD** = 0.0002 mg/kg/day | FQPA SF = 1<br>**cPAD** = chr RfD / FQPA SF<br>= 0.0002 mg/kg/d | Chronic/carcinogenicity study - rat<br>LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4. |
| Short-Term Oral (1-7 days)<br><br>(Residential) | oral study<br>LOAEL ≤0.1 mg/kg/day<br>UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation | **LOC for MOE** = 300 (Residential, includes the FQPA SF) | Developmental toxicity Study - rabbit<br>LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency. |

| | | | |
|---|---|---|---|
| Intermediate-Term Oral (1 week - several months)<br><br>(Residential) | oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation | **LOC for MOE** = 300 (Residential, includes the FQPA SF) | Developmental Toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency. |
| Short-Term Dermal (1-7 days)<br><br>(Occupational/ Residential) | dermal study NOAEL= 5 mg/kg/day | **LOC for MOE** = 100 (Occupational)<br><br>**LOC for MOE** = 100 (Residential, includes FQPA SF) | 21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes. |
| Intermediate-Term Dermal (1 week - several months)<br><br>(Occupational/ Residential) | dermal study NOAEL= 5 mg/kg/day | **LOC for MOE** = 100 (Occupational)<br><br>**LOC for MOE** = 100 (Residential, includes FQPA SF) | 21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes. |
| Long-Term Dermal (several months - lifetime)<br><br>(Occupational/ Residential) | oral study NOAEL= 0.019 mg/kg/day (dermal absorption rate = 1%) | **acceptable MOE** = 100 (Occupational)<br><br>**acceptable MOE** = 100 (Residential, includes FQPA SF) | Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4. |
| Short-Term Inhalation (1-7 days)<br><br>(Occupational/ Residential) | oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%) | **LOC for MOE** = 100 (Occupational)<br><br>**LOC for MOE** = 100 (Residential, includes FQPA SF) | Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary). |
| Intermediate-Term Inhalation (1 week - several months)<br><br>(Occupational/ Residential) | oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%) | **LOC for MOE** = 100 (Occupational)<br><br>**LOC for MOE** = 100 (Residential, includes FQPA SF) | Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary). |
| Long-Term Inhalation (several months - lifetime)<br><br>(Occupational/ Residential) | oral study NOAEL= 0.019 mg/kg/day (inhalation absorption rate = 100%) | **acceptable MOE** = 100 (Occupational)<br><br>**acceptable MOE** = 100 (Residential, includes FQPA SF) | Chronic/carcinogenicity rat study LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4. |
| Cancer (oral, dermal, inhalation) | Group C - possible human carcinogen | Use chronic RfD to estimate human risk | Increases in thyroid follicular cell tumors with fipronil (male/female) |

[1] UF = uncertainty factor, FQPA SF = FQPA Safety Factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, LOC = level of concern, MOE = margin of exposure.

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# R189616

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